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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,178	05/31/2006	Marta Garcia De La Torre	X-16440	3986

25885 7590 10/29/2007

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EXAMINER	
JARRELL, NOBLE E	
ART UNIT	**PAPER NUMBER**
1624	

NOTIFICATION DATE	DELIVERY MODE
10/29/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/581,178	DE LA TORRE ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,18,20 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16,18,20 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/31/2006; 10/18/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Current Status of 10 / 581178

1. Claims 15-16, 18, 20, and 23 are pending in the instant application and are being examined on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 15, 16, 18, 20, and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of the claimed compounds of claim 15, does not reasonably provide enablement for the solvates, enantiomers, and diastereomers of the compounds of claim 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants adequately show the preparation of each compound of claim 15. However, applicants are not enabled for the enantiomers and diastereomers of these compounds, because none of these compounds have asymmetric centers, which is a requirement for an enantiomer or diastereomers. (Daintith, J., *A Dictionary of Chemistry*, **1996**, pages 157 and 353-54). Applicants are also not enabled for solvates of these compounds. Vippagunta et al. (*Advanced Drug Delivery Reviews*, **2001**, *48*, 3-26) show that solvate prediction is unpredictable because each solid compound responds uniquely to the formation of solvate or hydrates, and hence generalizations cannot be made for a series of related compounds (section 3.4, page 18).

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858

F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to diaryl compounds that contain an ether linkage.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The compounds are not considered novel and the formation of solvates is unpredictable.

(5) The relative skill of those in the art:

One of ordinary skill in the art is familiar with the synthetic techniques shown in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the preparation of the compounds in claim 15.

However, the specification does not provide guidance for the formation of solvates of compounds of claim 15

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 15, 16, 18, 20, and 23, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 15, 16, 18, 20, and 23 are rejected under 35 U.S.C. 103(a) as being obvious over Blanco-Pillado et al. (WO 2004/026305, published 1 April 2004, filed 17 September 2003, claiming priority back to 60/412,158, filed 19 September 2002, provided in IDS) in view of Patani and LaVoie (*Chemical Reviews*, **1996**, *96*, 3147-76).

The applied reference has common inventors and a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37

CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Blanco-Pillado et al. teach species 1, 11, 17, 20, and 21 of claim 18, as well as species in claims 19 and 20. They also claim the hydrochloride, methanesulfonic, hydrobromide, bisulfate, and tartaric acid salts of these compounds in claim 25. Pharmaceutical compositions of these compounds are taught in claim 26. Claim 27 teaches the administration of these compounds to mammals. Claim 28 teaches the method of using these compounds in the treatment or prevention of obesity. This reference does not teach substitution of NH_2 for OH in a carboxylate group.

Patani and LaVoie teach that the NH_2 group can be substituted for the OH group in carboxylate groups (page 3168, section 3. Carboxylate Group Bioisosteres). It is stated that the determination of suitable replacements for the carboylate group is often based on the ability of the bioisostere to possess similar acidity and to exhibit similar physiochemical properties. It is also shown in this paper that the fluorine atom is a bioisostere of the H atom (table 4, page 3149). Even though the method of use in this paper is different than the instant intended use, there is motivation to substitute F for H on an aromatic ring. This reference does not teach compounds of claim 15.

The motivation for combining the teachings of these references arises form the fact that the compounds of Blanco-Pillado et al. are being used for the same purpose as the compounds of the instant claims. It is shown in the claims of the published application that the compounds are being administered to mammals requiring blocking of *mu*, *kappa*, and *delta*, receptors.

Claim 28 states that the method of use is for the treatment or prevention of obesity. It would be obvious to one of ordinary skill in the art to try these compounds in place of the instantly claimed compounds. Thus, claims 15-16, 18, 20, and 23 are rendered unobvious over Blanco-Pillado et al. in view of Patani and LaVoie.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 15,16,18, 20, and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 19, 20, 25, 26, 27, and 28 of copending Application No. 10/532960 in view of Patani and LaVoie.

Blanco-Pillado et al. teach species 1, 11, 17, 20, and 21 in claim 18 of 10/532960, as well as the species in claims 19 and 20 of 10/532960. The hydrochloride, methanesulfonic, hydrobromide, bisulfate, and tartaric acid salts of these compounds are recited in claim 25 of 10/532960. Pharmaceutical compositions of these compounds are taught in claim 26 of 10/532960. Claim 27 of 10/532960 teaches the administration of these compounds to mammals. Claim 28 of 10/532960 teaches the method of using these compounds in the

treatment or prevention of obesity. Copending application 10/532960 does not teach substitution of NH_2 for OH in a carboxylate group.

Patani and LaVoie teach that the NH_2 group can be substituted for the OH group in carboxylate groups (page 3168, section 3. Carboxylate Group Bioisosteres). It is stated that the determination of suitable replacements for the carboylate group is often based on the ability of the ability of the bioisostere to possess similar acidity and to exhibit similar physiochemical properties. It is also shown in this paper that the fluorine atom is a bioisostere of the H atom (table 4, page 3149). Even though the method of use in this paper is different than the instant intended use, there is motivation to substitute F for H on an aromatic ring. This reference does not teach compounds of claim 15.

The motivation for combining the teachings of these references arises form the fact that the compounds of Blanco-Pillado et al. are being used for the same purpose as the compounds of the instant claims. It is shown in the claims of the published application that the compounds are being administered to mammals requiring blocking of *mu*, *kappa*, and *delta*, receptors. Claim 28 states that the method of use is for the treatment or prevention of obesity. It would be obvious to one of ordinary skill in the art to try these compounds in place of the instantly claimed compounds. Thus, claims 15-16, 18, 20, and 23 are a case of non-statutory obviousness-type double patenting over Blanco-Pillado et al. in view of Patani and LaVoie.

This is a provisional obviousness-type double patenting rejection.

Allowable Subject Matter

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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